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A Severity Classification System for AIDS Hospitalizations

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A Severity Classification System for AIDS Hospitalizations

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The authors describe a new model for classifying hospitalized patients with acquired immunodeficiency syndrome (AIDS) according to their severity of illness. In the first phase of the project, a clinical model indicating the relative severity of AIDS complications was formulated, based on the clinical literature and expert opinion. In the second phase, the model was tested empirically using data on in-patient mortality of over 6,000 adult AIDS hospitalizations in New York State during 1985. The ordering of AIDS-related complications in the clinical model was revised to reflect a continuum of increasing likelihood of death in the hospital. The final classification system for AIDS hospitalizations has 20 substages, grouped into three stages, with in-patient mortality rates increasing from 6% to 60%. The system is automated and can be applied to different AIDS populations to analyze resource use and outcomes of hospital care. Key words: acquired immunodeficiency syndrome; severity of illness; classification system; AIDS hospitalizations; mortality rates; survival; nonopportunistic infections; complications; staging; computerized hospital discharge abstracts. (Med Care 1989; 27:423–437)

Efforts to study the epidemiology of acquired immunodeficiency syndrome (AIDS) and the differential burdens imposed by the epidemic on the health care system are hampered by the absence of a method for measuring severity of illness. Differences in the severity of hospital cases should be considered when comparing the costs and outcomes of health services. Such adjustments are important for prospective payment systems and quality surveillance.[1]

We define discrete severity levels for AIDS-related conditions in hospitalized AIDS patients. The classification system is derived from a clinical model that indicates the relative severity of common AIDS complications. The model incorporates information provided in published studies and the opinions of AIDS experts. The model also relies on principles used in the development of Disease Staging by Gonnella and colleagues.[2] The clinical model was tested with automated discharge abstracts of over 6,000 AIDS hospitalizations in New York in 1985. The final staging hierarchy reflects the con-

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fluence of medical judgment and in-patient mortality rates associated with single and multiple complications.‡

This classification system differs from other systems for AIDS because it: 1) focuses specifically on AIDS and is based upon an *a priori* model of the clinical severity of AIDS complications; 2) incorporates many common complications of the disease including some not yet deemed reportable by the Centers for Disease Control (CDC); 3) groups complications into three stages of 20 substages, with increasing mortality rates; and 4) uses readily available hospital discharge abstract data.

Other AIDS classification systems achieve different ends. While the CDC's surveillance definition has changed in response to new information on the effects of the human immunodeficiency virus (HIV) causing AIDS,[3-6] it includes primarily the most serious manifestations of the disease without taking into account relative severity. In contrast, the Walter Reed Staging Classification recognizes the severity of manifestations of HIV infection by focusing on very specific information, such as the effects of the HIV on the T-helper cell population.[7] However, these data are commonly available only in medical record-based data systems. Further, the Walter Reed system provides less detail regarding AIDS itself because it encompasses the entire spectrum of HIV infection, from high-risk contacts to opportunistic infections. Another widely used but limited classification simply categorizes AIDS patients into groups based on the presence of three or four common AIDS-related complications recognized by the CDC: Kaposi's sarcoma (KS) alone, *Pneumocystis carinii* pneumonia (PCP) alone, KS and PCP, and other opportunistic infections.[8,9] None of these systems categorizes AIDS hospitalizations according to relative severity of illness. The staging model described here is valuable because it classifies AIDS hospitalizations contained in automated data bases into well-defined groups with established differences in outcomes, measured by in-patient mortality.

‡ A computerized version of the final severity classification system is available from the National Technical Information Service (NTIS), Springfield, VA 22161; (703) 487-4650. The full distribution kit contains an overview manual, users' guide, computer programs, and related files. The kit is available in hard copy, magnetic tape, and diskette media under NTIS accession numbers PB88-249412, PB88-249404, and PB88-249396, respectively.

Methods

The goal of this study was an integrated staging system, permitting classification of AIDS-related complications along a single severity scale. The final classification of hospitalizations was accomplished through a multistep process that began with the development of a clinical staging model. The clinical model was translated into diagnosis codes used in automated discharge data. Empirical analyses of in-hospital mortality rates associated with AIDS-related complications also were conducted because of the lack of available information about the prognosis of complications of AIDS other than KS and PCP. The final classification, therefore, reflects a reordering of the clinical model after statistical analyses of the mortality rates and after comment by AIDS experts.

Development of a Clinical Model

Seven common complications of AIDS were identified by literature review. These included all four categories in the latest revision of the CDC surveillance case definition: wasting syndrome, secondary neoplasms, opportunistic infections, and dementia/encephalopathy.[3] Three additional categories commonly produce significant morbidity in AIDS patients: hematologic disease, other infectious diseases (termed: nonopportunistic), and organ failure.

Because each of the seven categories en-

compasses a broad range of severity, we divided them into clinically significant and relatively homogeneous subcategories of related conditions. For example, KS and specific lymphomas are significant components of the secondary neoplasms. Infectious diseases were divided by organ system and pathogenic organism (when known). Further details on the categories and subdivisions are presented below.

The clinical model of the severity of AIDS-related complications is shown in Table 1. The order reflects: 1) the principles of Disease Staging, 2) published research regarding the degree of immunosuppression and morbidity/mortality associated with each complication, and 3) opinions of AIDS experts who reviewed preliminary versions of the clinical model. The following sections describe these three sources further.

Disease Staging, developed by Gonnella and colleagues,[2] identifies severity levels for over 400 diseases based on a body system/etiology matrix. Panels of experts defined increased severity for each disease based on a conceptual model of the disease process. Staging for a disease establishes points towards increased morbidity and risk of death based on progression from minimal involvement of one organ to multiple or severe organ involvement, and finally, death. Typically, diseases are divided into four stages, with substages within each as needed.

Staging for AIDS must depart from this model because AIDS involves multiple organ systems and is complicated by many pathophysiologic processes. It is known to result from a devastating retroviral infection that destroys components of the immune system and predisposes patients to many neoplastic, infectious, and degenerative conditions.[10] One approach for recognizing the multidimensional aspects of AIDS would be to establish separate severity classifications for the most common complications. However, defining a staging system for one disease, KS, has been a difficult task.[11-13] Moreover, separate classifications would restrict comparisons of patients with diverse manifestations of the disease.

TABLE 1. Clinical Model of the Severity of Common AIDS Complications, Listed by Increasing Severity

- Stage 1. Longest survival and least morbidity
  - Hematologic disease alone[a]
  - Wasting syndrome alone
  - Any of the secondary neoplasms:
    - Kaposi's sarcoma, localized skin
    - Kaposi's sarcoma, diffuse skin or visceral
    - Specific lymphomas
  - Secondary neoplasm and wasting syndrome
- Stage 2. Reduced survival
  - Infections
    - Single nonopportunistic infection[a,b]
    - Stage 1 complication(s) with single nonopportunistic infection[b]
    - Single opportunistic infection[c]
    - Stage 1 complication(s) with single opportunistic infection[c]
- Stage 3. Poor survival and significant morbidity
  - HIV encephalopathy (AIDS dementia complex)
  - Infections
    - Multiple infections: nonopportunistic and opportunistic (excluding two or more opportunistic)[b]
    - Multiple infections: two or more opportunistic[c]
    - Central nervous system nonopportunistic infection (excluding septicemia)
    - Nonopportunistic septicemia
  - Vital organ failure

[a] This condition occurring alone does not meet Centers for Disease Control surveillance definition.
[b] Excludes central nervous system infection and septicemia.
[c] Excludes central nervous system infection, septicemia, and multiple infections.
AIDS = acquired immunodeficiency syndrome, HIV = human immunodeficiency virus.

Given the complexity of AIDS, the following principles used in Disease Staging were followed as closely as possible in the development of the clinical model. First, morbidity and mortality should increase with rising stage. Second, limited involvement of one organ is less severe than extensive involvement of one organ or the involvement of multiple organs with a disease process (such as an infection). Third, multiple complications are generally worse than single complications. Fourth, central ner-

vous system (CNS) disease and organ failure are associated with high mortality rates and advanced stage classifications.

Data from the clinical literature were also used to construct the model, and because the literature does not address the prognosis of all complications, physicians with expertise in the clinical manifestations of AIDS provided advice in this phase of the project. Stage 1 was distinguished from Stage 2 primarily by the absence of infections (Table 1). Patients with KS alone maintain a greater degree of immunocompetence and live longer than patients who have opportunistic infections.[9,10,14] Wasting syndrome (formerly part of AIDS-related complex, an AIDS prodrome), other neoplasms, or hematologic disease (e.g., thrombocytopenia) occurring alone during a hospitalization are considered more analogous to KS than to opportunistic infections in the degree of morbidity due to HIV infection and are placed in Stage 1.[14] Consonant with several staging versions for KS, this condition was subdivided by the extent and location of the disease and the presence of systemic (wasting) symptoms.[11-13]

Stage 2 included CDC-defined opportunistic infectious complications and nonopportunistic infections that are not recognized by the CDC case definition. These nonopportunistic infections increase morbidity and mortality in AIDS as they do in any other disease process (e.g., pneumococcal pneumonia in diabetes). Because nonopportunistic infections do not necessarily signify serious compromise of the immune system, they were not considered as severe as opportunistic infections. Finally, any infection accompanied by any noninfectious complication in Stage 1 is considered more severe than the infection occurring alone.

Stage 3 included the most severe infections, organ failure, and HIV encephalopathy (AIDS dementia complex). Although the CNS involvement with HIV infection can have many manifestations of varying severity, AIDS dementia complex usually occurs in advanced stages of infection when patients experience life-threatening infections.[15] It leads to progressive disability and can require full-time care for all bodily functions. As in the demented elderly patient, this condition can predispose patients to a wide variety of serious complications, and thus it warranted a high stage.

Study Population

The automated hospital discharge abstract records used in this study were provided by the New York Statewide Planning and Research Cooperative System (SPARCS Bureau). These data are particularly well suited for this application. The AIDS patients from New York State account for nearly one third of all AIDS patients nationally[16] and provide a large and heterogeneous mix of AIDS manifestations. In addition to patient demographic and billing data, each record contains a maximum of five diagnosis codes and five procedure codes as well as discharge disposition (dead, home, or transfer).

Determination of the appropriate ICD-9-CM diagnosis codes for identifying AIDS patients was essential. Before new guidelines became effective in October 1986, the National Center for Health Statistics, the American Medical Record Association, and the American Hospital Association recommended that AIDS be coded with ICD-9-CM code 279.19, "other deficiency of cell-mediated immunity." Telephone interviews with medical record coding managers of six major New York hospitals indicated that coders used 279.19 only when AIDS was listed as a specific diagnosis in the medical record. For this reason, this code was chosen as a deliberately conservative selection criterion to minimize the possibility of including non-AIDS patients with the same complications as AIDS patients. During this time period, patients testing HIV positive were coded as 795.7, "other nonspecific immunological findings." However, only 169 pa-

tients with the HIV infection code but without the AIDS code were found. Such patients were excluded from the study.

The initial data base for the study consisted of nearly 3 million discharge abstract records for patients hospitalized in New York State in 1985. Among these, approximately 6,900 records carried the 279.19 code in one of five diagnosis fields. Obstetric patients and those below 18 and above 64 years of age were deleted due to small sample sizes. The final analysis file contained 6,142 records. Demographic characteristics were consistent with those previously reported for AIDS patients in New York:[17,18] 86% of hospitalized AIDS patients were male; their average age was 36; and 44% were white.

The unit of analysis for this study was the hospitalization because information was not available to identify multiple hospitalizations of a single patient. Hence, most AIDS patients were likely to be reported more than once. Assuming that AIDS patients were hospitalized, on average, between two and three times during 1985,[19] the 6,142 records included in this study represent between two and three thousand persons. The inability to follow AIDS patients over time is an important limitation. When such data become available, they will provide a valuable resource for validating and extending the severity instrument described here. However, it is likely that confidentiality concerns, among other factors, will continue to restrict the construction of linked data files.

Operationalizing the Clinical Model

For application to automated data, the conditions included in the clinical model had to be translated into appropriate ICD-9-CM codes with the assistance of a medical records specialist. Some diseases (e.g., certain opportunistic infections) could not be coded as specifically as desired because ICD-9-CM classification generally does not indicate chronicity or exact sites involved. When possible, combinations of codes were used to improve precision.

Using the data file described above, ICD-9-CM codes were examined to identify conditions included in the clinical model that occurred with sufficient frequency for meaningful analysis. Codes appearing in the study population that had not been included in the ICD-9-CM translation of the clinical model were grouped by organ system and pathophysiologic process. Frequencies were examined to determine whether other important categories of complications could be defined. No additional major classes of diseases (e.g., neoplastic or vascular) occurred in sufficient numbers to warrant the inclusion of more categories, except for diagnoses included in the "mental disorders" chapter of ICD-9-CM. These were excluded explicitly because of our emphasis on medical, as distinguished from psychiatric, conditions. Moreover, more than three quarters of all mental disorders were related to sexual preference or drug abuse. Thus, medical judgments about which complications to include were not changed.

Development of Severity Classification Based on In-patient Mortality Rates

Mortality rates for patients grouped into the categories in the clinical model were analyzed and compared in an iterative process using two-tailed *t*-tests of significance at the 95% confidence level. First, mortality rates were calculated for patients with only one of the most common complications (other than the immunodeficiency condition) within each of the seven categories of AIDS complications. Then, mortality rates were calculated for groups of patients representing all possible combinations of complications. Since at least 1% of the population was necessary to produce robust estimates of mortality rates, groups were combined where appropriate. Groups were only col-

TABLE 2. Distribution of Selected AIDS-Related Complications, by Category

Description of Complication	Percent of Total Cases
Total (No. = 6,142)	100.0[a]
Wasting syndrome	7.7
Secondary neoplasms	
Kaposi's sarcoma	13.5
Lymphomas	2.0
Hematologic complications	23.9
Nonopportunistic infections[b]	
Single	29.5
Multiple	7.5
Central nervous system	1.9
Septicemia	5.2
Opportunistic infections[c]	
Pneumocystis carinii pneumonia	33.4
Single, non-PCP	24.5
Multiple	7.9
Dementia/encephalopathy	1.6
Organ failure	5.4

[a]Components do not add to the total due to the occurrence of multiple complications in a single case.
[b] Distinguished by number of sites or organ systems.
[c] Distinguished by number of organisms.
AIDS = acquired immunodeficiency syndrome.
Source: 1985 New York SPARCS Bureau data, Hospital Studies Program, National Center for Health Services Research and Health Care Technology Assessment.

lapsed when they fit the logic of the clinical model and also had similar mortality rates.

As a result of these analyses, single and multiple complications were reordered for the final severity classification system. Such changes were expected. The clinical model served as a framework for the empirical analyses and provided logical boundaries for limiting the reordering of complications across stages. The mortality rates were useful primarily in determining components of the three stages and establishing rankings within stage levels.

Results

Distribution of AIDS-Related Conditions

The seven categories of AIDS complications in the clinical model, their subcategories, and frequencies of occurrence in the analysis sample are displayed in Table 2. Four categories of conditions met the criterion for CDC-defined AIDS indicator diseases.[3] First was wasting syndrome, characterized by profound involuntary weight loss, chronic diarrhea or fever, and weakness with no etiology other than HIV infection. In the presence of infections (discussed below), the definition of wasting syndrome was restricted to weight loss or severe malnutrition. Conditions indicative of wasting syndrome were coded in 7.7% of the hospitalizations in our study. The second was secondary neoplasms, KS, and specific lymphomas including immunoblastic, small non-cleaved or Burkitt's, and primary lymphoma of the brain. Secondary neoplasms were identified in 15.1% of AIDS hospitalizations.

The third was opportunistic infections. Fourteen specific opportunistic infections are included in the latest CDC surveillance definition. They are PCP, chronic cryptosporidiosis, toxoplasmosis of the brain, extraintestinal strongyloidiasis, chronic isosoporiasis, extrapulmonary cryptococcosis, cytomegalovirus infection (other than liver, spleen, or lymph nodes), Herpes simplex (including chronic mucocutaneous, bronchitis, pneumonitis, esophagitis), recurrent *Salmonella* septicemia, progressive multifocal leukoencephalopathy, extrapulmonary tuberculosis or atypical mycobacterium infection (other than skin), extrapulmonary histoplasmosis, and candidiasis (other than thrush which is virtually ubiquitous in the AIDS population). Over half (54.3%) of AIDS hospitalizations in this study presented with infections caused by one or more opportunistic organisms. Although opportunistic infections were analyzed both by organism and by site, the former was found to be more reliable in differentiating homogeneous groups as measured by in-hospital mortality rates. Because of the relatively low morbidity associated with cutaneous infections (e.g., genital Herpes simplex), these conditions were analyzed only when patients had no other opportunistic infec-

tions. That is, when they occurred with other infections, cutaneous infections were not considered as additional co-morbidities. Patients with PCP had higher in-hospital mortality rates than patients with infections due to other opportunistic organisms with sufficiently large numbers to warrant special study. The other most common opportunistic organisms, *Toxoplasma gondii* (n = 121 or 2% of cases) and *Cryptococcus neoformans* (n = 181 or 3% of cases), did not have distinctive patterns of in-hospital mortality and were not categorized separately. Thus, three types of opportunistic infections were distinguished: PCP, single non-PCP organism, and multiple organisms (PCP and/or non-PCP); PCP was the single most common condition among hospitalized AIDS patients, infecting more than 33%.

The fourth CDC category was dementia/encephalopathy and includes encephalopathy, dementia, and myelopathy with no apparent etiology other than HIV infection. Diagnosis codes indicating dementia/encephalopathy were found in 1.6% of the study population.

Three additional categories of complications were analyzed. Two of these, hematologic disease and nonopportunistic infections, are not recognized by the CDC case definition, while the third, vital organ failure, may result from a combination of CDC designated and nondesignated conditions. Table 2 also displays frequencies of these categories of common complications. The first of these is hematologic disease (other than the primary effects of the HIV on lymphocytes) a widely recognized complication of AIDS that may be due to multiple etiologies including infectious, neoplastic, metabolic, and toxic.[20-23] Nearly one quarter of our study patients had nonhereditary forms of anemia, thrombocytopenia, agranulocytosis or neutropenia, or aplastic anemia. As the least severe hematologic complication, anemia alone was excluded in the presence of any infection because it did not significantly change in-hospital mortality.

The second was nonopportunistic infections, predominantly acute bacterial, viral, fungal, and protozoal infections not designated by the CDC as opportunistic infections and infections without a defined organism. Examples of these include: bronchopneumonia or urinary tract infections due to various organisms, bacterial septicemia (excluding *Salmonella*), pulmonary tuberculosis, and cellulitis due to an undefined organism. Over one third (36.9%) of hospitalized AIDS patients in this study had some type of nonopportunistic infection. The importance of these infections in AIDS patients is supported by both laboratory and clinical research. Patients with AIDS have been observed to have defective B-cell function which predisposes them to bacterial infections.[24,25] Infections other than those included in the CDC surveillance definition have been noted to cause significant morbidity and mortality in AIDS patients.[26-29] Nonopportunistic infections were analyzed only by organ site because organisms causing these infections cannot be identified reliably with ICD-9-CM diagnosis codes. These infections were subdivided further into groups accounting for maximum variation in mortality: single site, multiple sites, central nervous system, and septicemia. Table 2 displays the frequencies of the subgroups within the population.

The final category was organ failure. Conditions indicating severe compromise or failure of the respiratory, renal, cardiac, or hepatic organs were included as the most severe consequences of AIDS and also are described in a variety of studies.[30-35] Approximately 5% of patients experienced some type of organ failure; the most common form was respiratory, primarily following PCP or bacterial pneumonia.

The Staging System Overall

The AIDS staging system is shown schematically in Figure 1. Each substage is defined by an essential condition (represented

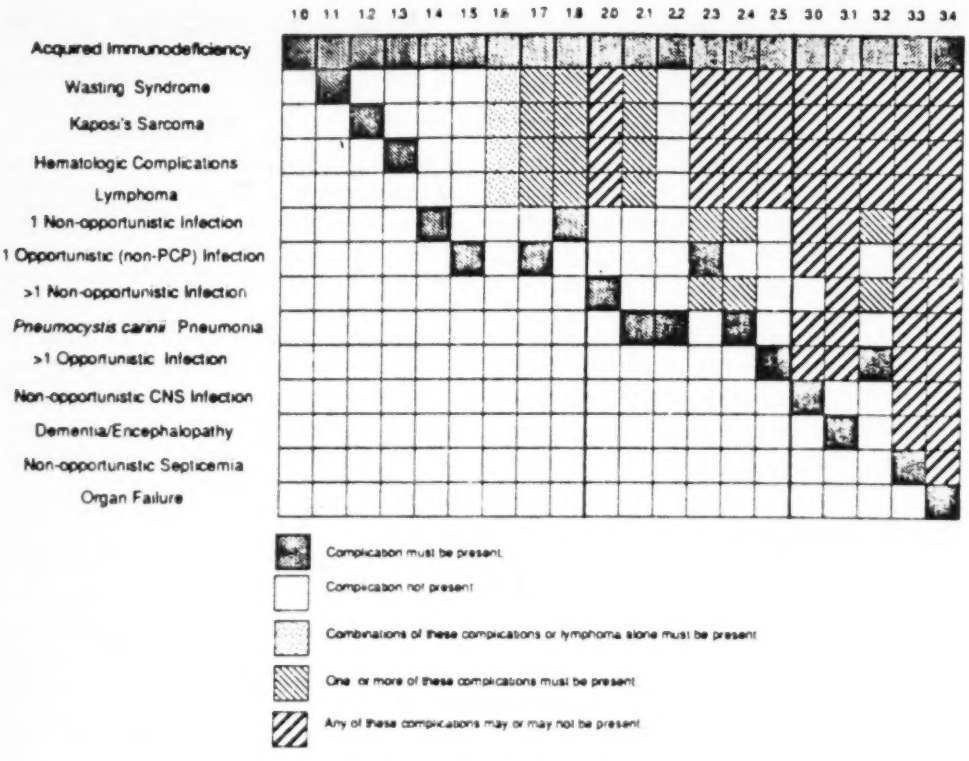
10 11 12 13 14 15 16 17 18 20 21 22 23 24 25 30 31 32 33 34
Acquired Immunodeficiency
Wasting Syndrome
Kaposi's Sarcoma
Hematologic Complications
Lymphoma
1 Non-opportunistic Infection
1 Opportunistic (non-PCP) Infection
>1 Non-opportunistic Infection
Pneumocystis carinii Pneumonia
>1 Opportunistic Infection
Non-opportunistic CNS Infection
Dementia/Encephalopathy
Non-opportunistic Septicemia
Organ Failure
Complication must be present
Complication not present
Combinations of these complications or lymphoma alone must be present
One or more of these complications must be present
Any of these complications may or may not be present

FIG. 1. AIDS staging system.

by black boxes) which is a prerequisite for classification into that substage. The essential condition may occur alone or in combination with secondary co-morbidities. About one half of all hospitalizations in our study had only one complication. Separate substages were established for the most frequently occurring single complications: wasting syndrome, KS, hematologic conditions, PCP, and other infections occurring alone.

Twenty distinct substages of AIDS hospitalizations were defined within three stages. Stage 1 included single or multiple noninfectious complications (wasting syndrome, hematologic disease, secondary neoplasms) or a single infection other than PCP which may be accompanied by any noninfectious complication. The average mortality rate for patients in Stage 1 was 12.6%. Stage 2 included PCP alone or associated with noninfectious complications, and multiple infections within the opportunistic or nonopportunistic groups. Patients in Stage 2 had an average mortality rate of 24.5%. Included in Stage 3 were central nervous system infections, dementia/encephalopathy, combinations of multiple opportunistic and nonopportunistic infections, septicemia, and organ failure. On average, more than half (51.5%) of Stage 3 patients died in the hospital.

The number of hospitalizations associated with each substage and corresponding in-hospital mortality rates are reported in Table 3. The mortality rates are displayed graphically by substage in Figure 2. Within each stage level, the substages were ordered by mortality rates. Only three substages

TABLE 3. Distribution of AIDS Hospitalizations and Mortality Rates, by Substage

Stage and Description*	Number of Cases	Percent of Cases	Mortality Rate
Total	6,142	100.0	22.5
Stage 1			
1.0 Unclassified	631	10.3	11.4
1.1 Wasting syndrome only	100	1.6	6.0†
1.2 Kaposi's sarcoma only	240	3.9	8.3
1.3 Hematologic disease only	237	3.9	10.5
1.4 One nonopportunistic infection only	665	10.8	12.2
1.5 One non-PCP opportunistic infection only	596	9.7	12.9
1.6 Combinations of 1.1-1.3 &/or lymphoma	168	2.7	15.5
1.7 One non-PCP opportunistic infection + NIC	160	2.6	15.6
1.8 One nonopportunistic infection + NIC	191	3.1	19.9
Stage 2			
2.0 More than one nonopportunistic infection	162	2.6	17.3
2.1 PCP + NIC	256	4.2	17.6
2.2 PCP only	875	14.2	23.2†
2.3 One non-PCP opportunistic infection + NOI	279	4.5	24.7
2.4 PCP + NOI	323	5.3	27.2
2.5 More than one opportunistic infection	339	5.5	30.4
Stage 3			
3.0 Nonopportunistic central nervous system infection	104	1.7	34.6
3.1 Dementia/encephalopathy	87	1.4	37.9
3.2 More than one opportunistic infection + NOI	112	1.8	42.9
3.3 Nonopportunistic septicemia	286	4.7	54.9†
3.4 Organ failure	331	5.4	60.4

* Descriptions of patient groups highlight only the distinguishing features of each substage. They are of the general form: "essential condition + secondary condition(s)." Secondary conditions include: "NIC," any of the noninfectious complications (wasting syndrome, secondary neoplasms, and/or hematologic disease); and "NOI," nonopportunistic infection(s).

† Statistically significant difference from mortality in preceding substage at a 95 percent level of confidence.

AIDS = acquired immunodeficiency syndrome, PCP = *Pneumocystis carinii* pneumonia.

Source: 1985 New York SPARCS Bureau data, Hospital Studies Program, National Center for Health Services Research and Health Care Technology Assessment.

disrupted the pattern of monotonically increasing mortality rates.

Unstaged Hospitalizations—Substage 1.0

The overall mortality rate for Stage 1 is somewhat overstated because 631 unclassified AIDS hospitalizations (10.3% of the study population) were placed in substage 1.0. Patients placed in this substage either had no co-morbidity listed on their discharge abstract record (2.8% of the total population) or their co-morbidities occurred so infrequently that a separate substage could not be defined (7.5% of the total population). Patients with the immunodeficiency code as the sole diagnosis, constituting 27.4% of unstaged hospitalizations, had an average mortality rate of 13.9%. Another 16.8% of unstaged hospitalizations had an additional diagnosis of thrush, and the mortality rate for these patients was 5.7%. Patients with mental disorders (other than dementia) were 24.4% of unstaged hospitalizations; their mortality rate was 6.5%. In the remaining 31.4%, no diagnoses were represented sufficiently to warrant separate analyses, and these hospitalizations had a combined mortality rate of 16.2%. Examples of these miscellaneous diagnoses included diabetes mellitus and hypertension.

Stage 1

As expected from other studies of the morbidity and mortality associated with

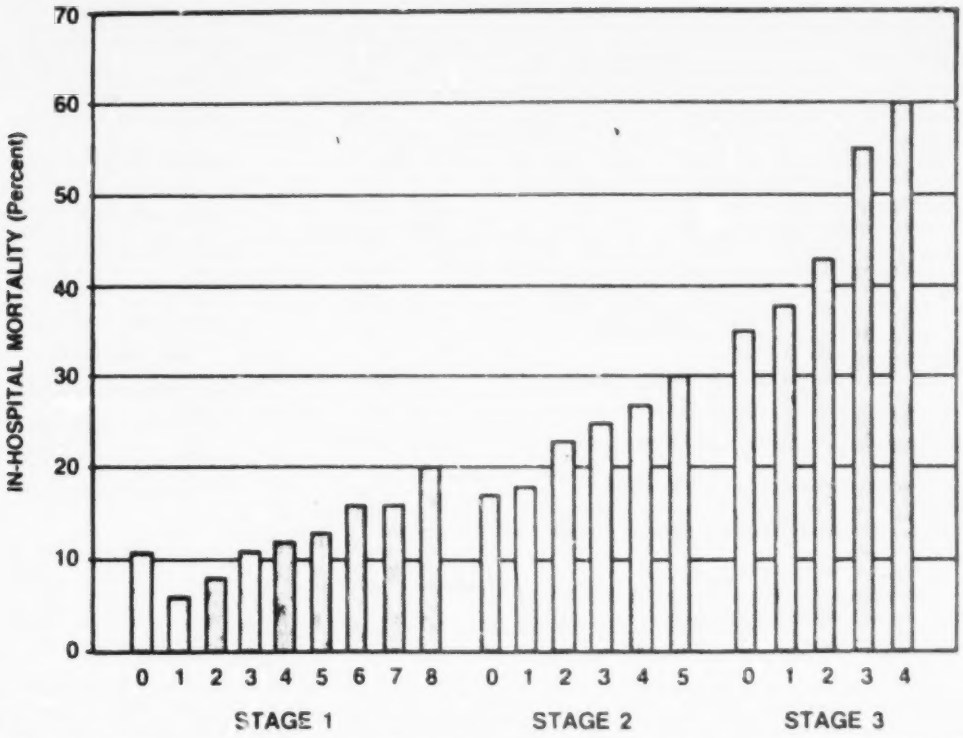

FIG. 2. In-hospital mortality rates for AIDS hospitalizations, by substage. (Source: 1985 New York SPARCS Bureau data, Hospital Studies Program, National Center for Health Services Research and Health Care Technology Assessment.)

AIDS complications, the following single noninfectious complications had low mortality rates (Table 3): wasting syndrome, KS, hematologic disease, and lymphoma. Patients with all forms of KS were combined in substage 1.2 because separate analyses indicated that their mortality rates did not differ for localized versus diffuse or visceral disease. This may have been due to inexact ICD-9-CM coding of the extent of the disease or because hospitalized KS patients are a relatively homogeneous group. The lymphoma patients had the highest mortality rate of these complications, 15.5%.

Stage 1 includes four substages with infectious complications. The clinical model predicted a significant increase in mortality associated with opportunistic infections in comparison to noninfectious complications, but this was not observed for infections other than PCP. As shown on Table 3, non-PCP opportunistic infections conferred mortality rates that were similar to those associated with single nonopportunistic infections (e.g., substages 1.4 and 1.5). Thus it is possible that although these opportunistic infections have grave implications for long-term prognosis, they may not differ significantly from other types of infections in short-term prognosis.

Over 60% of the nonopportunistic infections comprising substage 1.4 involve the respiratory system. Because of an increasing recognition that interstitial pneumonitis is a manifestation of AIDS in adults,[36] the 258 patients with this condition were analyzed

separately. However, their average in-hospital mortality rate did not differ from those for other groups of patients in substage 1.4.

Patients with infections accompanied by one of the noninfectious complications in Stage 1 had higher mortality rates than patients with infections without such complications. In fact, a surprisingly high mortality rate—19.9%—was observed for patients in substage 1.8 who had one or more of the Stage 1 noninfectious complications and one nonopportunistic infection. This group was maintained in Stage 1 because it was considered important to maintain a distinction between PCP and all other single infections in the model.

Stage 2

We noted that PCP conferred the highest mortality rate of all opportunistic or nonopportunistic infections (excluding CNS and disseminated). This high mortality rate was expected based on clinical studies. However, contrary to the clinical model, when PCP occurred as the only diagnosis (other than immunodeficiency), the in-patient mortality was significantly higher than when PCP was combined with any of the Stage 1 noninfectious conditions, such as KS (23.2 vs. 17.6). This distinction had not been made in the clinical model since most studies do not note significant differences between the survival of patients with KS who develop PCP and those with PCP alone. However, this finding has been observed in a few studies.[9,37] Rothenberg et al.[9] reported longer median survival with PCP and KS than for PCP alone (381 vs. 318 days, respectively). This finding also held when measured in terms of 1-year cumulative survival probabilities.

In substages higher than 2.2, PCP alone, the presence or absence of noninfectious complications, such as neoplasms, does not appear to affect in-hospital mortality. However, as expected in the clinical model, when nonopportunistic infections complicate an opportunistic infection (PCP or non-PCP), a higher mortality rate was observed consistently. Substage 2.3 included cases with an infection due to one non-PCP opportunistic organism and a nonopportunistic infection and had a mortality rate of 24.7%. Substage 2.4, PCP combined with a nonopportunistic infection, had a mortality rate of 27.2%.

Infections due to two or more opportunistic organisms are consistently worse than two or more infections with only one secondary to an opportunistic organism and the other(s) to nonopportunistic organisms. Substage 2.5 includes patients with two or more opportunistic infections (which may include PCP), regardless of noninfectious complicating conditions. This substage has an in-hospital mortality rate of 30.4%.

Stage 3

Some of the highest mortality rates were conferred by multiple nonopportunistic infections, those which involve the CNS or are disseminated (septicemic). In substages 3.0, 3.2 and 3.3, mortality rates were observed to be 34.9%, 42.9%, and 54.9%, respectively. Surprisingly, CNS opportunistic infections were an exception with much lower mortality rates, and these were collapsed into the non-PCP opportunistic infection group.

Encephalopathy (AIDS dementia complex) was associated with a very high mortality rate—37.9%—probably because patients who have AIDS and are given a code for dementia have severe, disabling disease. Because of the imprecision of the ICD-9-CM codes, we cannot be assured that HIV infection was the reason for the dementia. To reduce the possibility that other infections were causing the condition, patients with CNS infection with other organisms or multiple or severe (disseminated) infections were excluded from substage 3.1.

Finally, as is usually observed in Disease Staging, failure of the cardiovascular, respiratory, hepatic or renal organ systems, sub-

stage 3.4, was associated with a 60% in-hospital mortality rate. The high mortality rates associated with these codes confirm that organ failure was being coded appropriately. For example, patients with respiratory failure were likely to have severe hypoxemia and respiratory compromise.

Discussion

The automated classification system reported in this paper was designed to distinguish clinically distinct groups of AIDS patients based on their in-patient mortality rates. A clinical model of increasing severity of AIDS-related complications, followed by analyses of in-patient mortality rates, guided the development of the classification system. Mortality rates associated with a continuum of 20 substages rose from 6% in the lowest substage, wasting syndrome, to 60% for the highest substage, organ failure. This classification was created to serve as a tool for analyses of in-patients with AIDS.

Notable differences between the final classification and initial clinical model center primarily on shifts in the hierarchy between Stages 1 and 2. Among the opportunistic infections, only PCP was associated with significantly higher in-patient mortality rates than all other types of infections occurring alone. Although other opportunistic infections present serious implications regarding the degree of immunodeficiency of an HIV-infected patient, they may alter an AIDS patient's risk of in-patient mortality no more seriously than, for example, an episode of bacterial pneumonia. In general, patients with an infection coupled with secondary neoplasms, hematologic disease, or wasting syndrome had slightly higher mortality rates than patients with no recorded complications apart from an infection. However PCP was an exception to this observation because patients with PCP and a Stage 1 noninfectious complication, such as KS, had a lower mortality rate than patients with PCP without any other complication. Possibly this was due to the fact that patients with KS were more likely to be homosexuals who may be less severely ill than patients without KS who may be more likely be intravenous drug abusers.[38]

The major factor contributing to the prediction of in-patient mortality was the number and type of infections contracted by an AIDS patient. In addition to the CDC-defined opportunistic infections, the presence of infections not recognized in the CDC surveillance definition consistently increased mortality rates for all conditions. Our data indicate that these nonopportunistic infections occurred frequently in this population, complicating 40% of hospitalizations in the study. For the most part, these infections were bacterial in origin. Further analyses of the patterns of these complications may lead to revisions of the CDC surveillance definition of AIDS. Clinicians should, in the meantime, be aware of the frequent occurrence of such infections in AIDS patients.

The inclusion in the classification system of nonopportunistic infections and other conditions not recognized by the CDC case definition greatly expanded the number of AIDS hospitalizations that could be classified. Had hospitalizations with only the AIDS code and CDC indicator diseases been included, 20% to 30% would have remained unclassified. With the integration of nonopportunistic infections, hematologic diseases, and some forms of organ failure, all but 7.5% of hospitalizations with comorbidities were classified.

Our classification system represents a research tool for use in future studies of hospitalized AIDS patients using other data bases. This model has been used in analyzing resource use by AIDS patients hospitalized in New York.[39] With rare exceptions, length of stay and total charges increased steadily with rising stage. Thus, the model can be used to control for variations in the severity of AIDS patients when analyzing automated hospital data.

The system also facilitates systematic monitoring of the types of conditions experienced by AIDS patients and the outcomes of these conditions. It can be used to assess quality of care by detecting groups of patients whose lengths of stay or in-patient mortality rates fall outside the norm for clinically similar patients. Innovations in in-patient care, such as dedicated AIDS units, can be studied by using this system to define clinically similar patient groups.

For these types of studies, data on clinical complications experienced by AIDS patients need not be obtained through automated sources. Clinical information from chart review, patient interviews, or other sources can be staged, probably with greater fidelity to actual conditions than is possible with ICD-9-CM codes. In addition, laboratory and clinical data such as those integrated into the Walter Reed Staging Classification may be used to refine and revise our staging classification. Still it is important not to overlook the value of automated hospital discharge abstract data in AIDS research, as such information has been relatively untapped for monitoring the progression and costs of the epidemic.

Future use of this classification should be undertaken only after the limitations of this study are recognized. First, this study relied exclusively on data for hospitalized patients. Persons with AIDS who are not treated in hospitals may have manifestations of the infection different from those found to be most important in this study. For example, failure to find differentiable subgroups among KS patients may reflect their more frequent treatment on an out-patient basis. Second, some records had little diagnostic information, e.g., some had the AIDS code alone, so we were unable to place these patients into meaningful categories. Over one fourth of the unstaged patients fell into this group. Third, the ICD-9-CM codes often do not provide the necessary specificity about disease processes, and they may not reflect fully important clinical differences among patients.[40] Automated medical records[1] would provide more comprehensive information and greater clinical specificity, but such data bases are still experimental and not generally available to researchers. Fourth, the SPARCS data contain only five diagnosis fields. More than one half of the hospitalizations in this study had all five diagnosis fields filled, indicating that other relevant classification information was excluded for want of space.

Fifth, the measure of severity of in-patient mortality does not capture all AIDS-related deaths nor does it reflect morbidity or changes in clinical status. Although 80% of known AIDS patients in New York die in the hospital,[41] certain types of patients may be more likely to be hospitalized or to remain in the hospital until death. Since 1985, the year of the hospital discharges used in this study, hospice and other out-patient care programs have been established to provide alternative sites for terminal care. In the future, it will be increasingly important to link patient death certificates to hospital data sets to examine mortality rates.

Finally, hospital discharge data generally have a lag time until they are available. Thus, analyses are frequently only possible with data that are several years old, as in this study. This represents a significant constraint in studying AIDS because the disease is undergoing rapid changes in its recognized clinical manifestations, treatment, and survival. In recent years, the survival of patients with some of the conditions integrated into the staging system has changed. The prognosis of patients with PCP has improved while that of patients with KS has worsened.[42,43] Further, the mortality data used in developing this staging system predates the widespread use of drugs that can improve the survival of AIDS patients. The staging system is currently being used in other, more recent data bases and is likely to continue to evolve in the same way that the CDC surveillance definition has changed in recent years.

Despite the limitations noted above, it is still clear that this classification and other methods are necessary to study patients who are comparably ill when examining clinical and economic outcomes of care. Automated discharge abstract data are essential in severity, clinical outcome, and reimbursement analyses. Widespread use of such a tool can promote understanding of the disease process itself and the costs and quality of care received by AIDS patients across the nation.

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